Clinical and Experimental Dermatology 1987; 12: 270–272.

Short course bifonazole therapy in pityriasis versicolor

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Accepted for publication 26 *September* 1986

Summary

Ninety patients were randomly assigned to one of three treatment regimens for pityriasis versicolor consisting of a once daily application of bifonazole 1% solution for a single day, 2 days (day one and day three) or 3 days (day one, day three and day six). Overall clinical cure rates 3 weeks after the end of therapy ranged from 69·9% to 89·9%. Statistical analysis showed a significant difference ($p \leqslant 0{\cdot}04$) in favour of three days therapy at the assessment three weeks and 90 days after the end of therapy. Short-term therapy with three applications of bifonazole seems to be effective in most cases of pityriasis versicolor, and needs to be compared against alternative forms of antifungal therapy.

Bifonazole (Mycospor) is a broad spectrum topical imidazole compound developed by Bayer AG, Germany, which has shown a high degree of *in vitro* activity against *Pityrosporum* spp. yeasts.[1] It is also effective *in vivo* in the treatment of pityriasis versicolor when used daily for 2 weeks, either as 1% cream, solution or gel.[2–4] A pilot study (R. J. Hay, personal communication) in nine patients has indicated that a single application of bifonazole 1% solution may be sufficient to treat pityriasis versicolor. The likelihood of patient compliance is increased by minimizing the daily frequency of topical applications and by shortening the duration of therapy.[5] For these reasons we have compared three different regimes of bifonazole 1% solution to study the efficacy of shorter courses of topical therapy in patients with pityriasis versicolor.

Patients and methods

Patients with pityriasis versicolor confirmed by direct microscopy of skin scrapings using the Parker-ink/potassium hydroxide method[6] were randomly assigned to one of three treatment regimes with bifonazole 1% solution. The study was arranged to test and compare the efficacy of bifonazole using three different treatment regimes. The medication was applied once daily at bedtime, was spread thinly and evenly to the affected areas of the skin and then rubbed in. Three groups, each comprising 30 patients, were tested. Group 1 was treated with a single application of the medication, Group 2 received a once daily application on day 1 and day 3 and Group 3 was treated on day 1, day 3 and day 6. Written consent was obtained from each patient. All patients were assessed prior to treatment by a detailed history and clinical examination. Five parameters of clinical disease activity (erythema, itching, scaling, hypo or hyperpigmentation) were assessed and scored as positive or negative. Patients who had received systemic or topical antifungals within one month prior to the study, or who had hypersensitivity to any of the imidazole group of drugs, or those with concomittant or mixed skin infections requiring antibiotics, were excluded from the trial.

The patients were assessed 3 weeks and 3 months after the end of therapy. At the first visit post therapy (3 weeks), the response was evaluated by correlating the clinical and microscopic findings. These were graded in the following categories: clinical cure with negative microscopy; clinical cure with positive microscopy; clinical improvement (mild scaling confined to a much smaller area compared to its pretreatment size) with positive microscopy; therapeutic failure (no clinical response to therapy) with positive microscopy and finally relapse was defined as signs of worsening pityriasis with positive microscopy in patients who had healed or improved after treatment. Any adverse effects were also recorded.

The clinical characteristics and history of patients included in the study are shown in Table 1. No significant differences between the three groups of patients were found in terms of age, sex, history of pityriasis versicolor, concomittant medication such as steroids and immunosuppressives and underlying diseases.

Results

Results of the assessment 3 weeks after the end of therapy

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Table 1. Characteristics of patients

Group	Number of patients (males, females)	Age of patients (years) Range	Mean	Number of patients 1st episode of P.V.	Duration of 1st episode (months) Range	Mean	Number of patients recurrent P.V.	Duration of actual episode (month) Range	Mean
1*	18, 12	16–62	31·3	14	1–44	17·07	16	1–6	4
2†	11, 19	14–61	29	10	1–60	10·7	20	1–60	5·6
3‡	19, 11	16–76	32	19	1–48	9	11	1–6	2·7

* One diabetic; one chronic alcoholism; one kidney transplant + steroids and immunosuppressors.

† One toxic oil syndrome.

‡ One acute lymphoid leukaemia + steroids; one chronic hepatitis + steroids; one kidney transplant + steroids and immunosuppressors.

Table 2. Pityriasis versicolor treated with bifonazole. Assessment 3 weeks after the end of therapy

	Number of patients		
	Group 1	Group 2	Group 3
Number of days treatment	1	2	3
Examined	30	30	30
Clinical cure/KOH negative	18 (60%)	19 (63·3%)	25 (83·3%)
Clinical cure/KOH positive	4 (13·3%)	2 (6·6%)	2 (6·6%)
Improvement/KOH positive	8 (26·6%)	9 (30%)	3 (10%)

Table 3. Assessment 90 days after the end of therapy

	Number of patients		
	Group 1	Group 2	Group 3
Examined	29	29	30
Clinical cure/KOH negative	23 (79·3%)	22 (75·86%)	27 (90%)
Clinical cure/KOH positive	0	0	0
Improvement/KOH positive	0	0	0
Relapses	6 (20·6%)	7 (24·14%)	3 (10%)

are shown in Table 2. All the patients in the three treatment groups showed a response to therapy: seventy patients were clinically cured but eight had positive microscopy and twenty showed marked improvement with positive microscopy. Results of the assessment 90 days after the end of therapy are shown in Table 3. Seventy-two patients were clinically and mycologically cured. Amongst these cured patients were four who had underlying diseases or had received concomittant medication (chronic hepatitis on systemic steroids, kidney transplant on immunosuppressives and steroids, diabetes and chronic alcoholism). Sixteen patients relapsed of whom two had underlying diseases (toxic oil syndrome, acute lymphoid leukaemia on steroids). The assessment 3 weeks after the end of therapy of those patients who had relapsed is shown separately in Table 4.

Side-effects were experienced by five patients: one patient in Group 1, three patients in Group 2 and a further patient in Group 3 had mild burning several hours after the application of the medication.

Statistical analysis using Student's t-test comparing Groups 1 and 2 showed no signficant differences in the clinical and mycological results 3 weeks after the end of therapy ($P \leqslant 0{\cdot}7$). But there was a significant difference ($P \leqslant 0{\cdot}04$) in favour of Group 3, when it was compared with Group 1 and 2. The low relapse rate of Group 3 at the assessment 90 days after the end of therapy was also significant ($P \leqslant 0{\cdot}04$). It seems, therefore, that short-term therapy with three applications of bifonazole seems to be more effective.

Table 4. Assessment 3 weeks after the end of therapy of the 16 relapses 90 days post therapy end

	Number of patients		
	Group 1	Group 2	Group 3
Clinical cure/KOH negative	2	3	3
Clinical cure/KOH positive	2	1	0
Improvement/KOH positive	2	3	0

Discussion

This study has confirmed the findings of R. J. Hay (personal communication), in a pilot study: namely that patients with pityriasis versicolor could achieve remission following a single application of bifonazole solution. In a previous randomized comparative study[7] no difference was found in terms of efficacy when two treatment regimes consisting of a daily application of bifonazole for one week were compared with the 2-week standard regime. The mycological cure rates in this study are similar to those found by other workers[2–4] using bifonazole 1% o.d. for 2 weeks. However, positive mycological findings at the assessment 3 weeks after the end of therapy do not necessarily presage treatment failure at the assessment three months after the end of therapy, as many of these patients appear to achieve remission without further therapy. Hence some patients rated as clinically, but not mycologically, cured at the assessment 3 weeks after the end of therapy and some rated as improved with positive microscopy, had achieved complete cures (clinical and mycological) at the assessment 90 days after the end of therapy.

In an *in vitro* and *in vivo* study with guinea-pigs infected with *T. mentagrophytes*[8], it has been shown that the uptake of bifonazole by this organism proceeds rapidly and that the compound remains within the pathogen at a concentration of at least 50% of the Minimum Cidal Concentration (MCC) for over 120 h. It is likely that antifungals which penetrate and persist in target organisms in this fashion will be particularly advantageous for short-term therapy, and this could explain the results of our study and the results of the pilot study mentioned previously.

There are two main approaches to the treatment of pityriasis versicolor. According to the first, it is necessary to eradicate as many pathogens (*M. furfur*) as possible, using intensive treatment. The opposing view is that *Pityrosporum* yeasts are saprophytes of the skin which shift to the pathogenic mycelial form (*M. furfur*) under the influence of different conditions and the object of treatment, which may be achieved by short courses of therapy, is to facilitate the reversal of this phase change rather than to destroy all organisms.

Patient compliance in topical therapy is increased if the frequency of applications is minimized and the duration of therapy shortened[6], although this is not universally accepted.[9] In the treatment of pityriasis versicolor, patient compliance is likely to be a problem because of the extensive nature of the infection and therefore short regime schedules, such as those discussed here, ought to be advantageous. However, more clinical experience is needed in addition to comparative studies of short courses of bifonazole and other alternative forms of therapy.

Acknowledgments

We would like to acknowledge the assistance of Bayer A.G. for supplies of bifonazole.

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